

REMARKS

Amendments to the abstract represent addition of information designating the depository, accession number, and deposit date of the deposited Huh-7.5 cell line in ATCC as per the requirements of 37 CFR 1.809(d). The insertion of such information in the specification after the filing date does not violate the prohibition against new matter in 35 U.S.C. §132 (see MPEP §2406.01, citing *In re Lundak*, 773 F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985)). Applicants also note that the statements of Jennifer Balsarotti and Dr. Keril Blight supporting the deposit of the Huh-7.5 cell line under the provisions of 37 CFR 1.809 (b) have been filed with the Patent Office. These statements were made by individuals in a position to corroborate that the Huh-7.5 cell line which is deposited is the Huh-7.5 cell line specifically identified in this Application and in the Applications to which this Application claims priority (i.e. Patent Application No. PCT/US2003/36634, filed November 13, 2003, and U.S. Provisional Application No. 60/426,256, filed November 13, 2002).

Amendments to the specification represent nothing more than the insertion of assigned sequence identifiers as per 37 CFR § 1.821(d). No new matter is introduced by these amendments. Applicants note that the underlined sequences shown in amended Table I were also underlined in the Table as originally filed and do not represent insertions of new sequences. A new Sequence listing that provides the peptide sequence of Genbank Accession no. AJ238799 as SEQ ID NO:27 has also been prepared using the AJ238799 sequence present in the Genbank database at the time that U.S. Provisional 60/426,256, to which the instant Application claims priority, was filed.

Claims 1-38 were presented in the original Application. Claims 1-9, 11, 16-32, 37 and 38 have been canceled. Claims 1-15 were previously presented. Claims 10 and 33-36 are currently amended and claims 39-41 are new. Claims 37 and 38 are cancelled without prejudice to the Applicants right to pursue such claims in subsequent continuations of this Application.

Support for the amendments to the claims can be found as follows. For “(A)n Huh-7.5 cell line on deposit with the ATCC as accession number PTA-8561” in Claims 10 and 33, Applicants note that addition of information designating the depository, accession number, and deposit date of the deposited cell line in ATCC after the filing date does not violate the prohibition against new matter in 35 U.S.C. §132 (see MPEP §2406.01, citing *In re Lundak*, 773 F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985)). For “obtaining a culture of said cell line that supports replication of said genomic or subgenomic HCV RNA” in Claim 10, support can at least be found in Examples 9, 10, and 11 of the specification. For “wherein said curing comprises treatment with an antiviral agent”, support can at least be found in Claim 11 as originally filed. For “S2204V, or S2204A” in Claim 36 and Claim 41, support can at least be found on Page 19, lines 1-16. Support for new Claims 39-41 can at least be found in Example 11.

SUMMARY OF OCTOBER 4, 2007 INTERVIEW

On October 4, 2007, the Applicant’s representative conducted a telephonic interview with Examiner Zachariah Lucas. Perfection of the Applicant’s priority claim to the November 13, 2002 filing date of U.S. 60/426,256 was first discussed, noting that the Applicants included this priority date on the Transmittal Letter accompanying the national stage filing of this Application and that “United States of America 60/426,256 11/13/2002” was listed under Foreign

Applications on the Filing Receipts of January 17, 2006 and May 9, 2006. Examiner indicated that the Office would likely accept this as evidence that the Office recognized the priority claim.

Proposed amendments to the claims 1 to 41 were also discussed. Examiner indicated that that claims specifically directed to the Huh-7.5 cell line and methods of it's use (i.e. claims 10-15, 33-36 and 39-41) were not anticipated by DeFrancesco et al. (WO 02/059321). Examiner alleged that Claim 38 was not enabled. Examiner also indicated that a screening or selection step should be added to Claim 10 to address the 35 U.S.C. §112, 1st paragraph rejections as per the Office Action of July 9, 2007 and further indicated that the Genbank accession number of Claims 36 and 41 should be replaced with a SEQ ID NO.

The disclosure of WO 01/89364 in Example 2 of Interferon Treated Cell Lines was also discussed. Examiner indicated that this publication was not considered to be prior art against the current claims. Applicants representative pointed out that since the WO 01/89364 publication was by the same inventive entity as this Application and occurred less than a year before the Applicants priority date of November 13, 2002, WO 01/89364 did not qualify as prior art under any section of 35 U.S.C. §102.

Statements supporting a deposit of biological material after the effective filing date under 37 CFR §1.804(b) were also discussed, with the Examiner indicating that such statements should be executed by individuals who were in custody of the material.

PRIORITY

In the Office Action of July 9, 2007, the Examiner alleged that the Applicant failed to comply with conditions necessary for receiving the benefit of an earlier filing date. Specifically,

the Examiner alleged that the the Application failed to provide the required reference under 37 C.F.R. §1.78 to prior U.S. Provisional Patent Application U.S. 60/426,256, filed November 13, 2002.

Applicants note that this priority date was included on the Transmittal Letter accompanying the national stage filing of this application and that "United States of America 60/426256 11/13/2002" was listed under Foreign Applications on the Filing Receipts of January 17, 2006 and May 9, 2006. The Patent Office's Notification of August 8, 2005 also listed a priority date of 11/13/2002. Applicant further notes that a certified copy of the Priority Document (i.e. U.S. Provisional Patent Application US 60/426,256) was provided to the Office on May 11, 2005. Although the Examiner indicated in the interview that the Patent Office would likely accept these documents as evidence that the Office recognized the priority claim, Applicants have nonetheless submitted a reference to the parent Applications to which priority is claimed (see Amendments to the Specification in this response), a Petition to Accept Unintentionally Delayed Claim to Priority under 37 C.F.R. §1.78(a)(3) (copy enclosed), and the surcharge specified by 37 C.F.R. §1.17(t) to obtain the benefit of the priority date of U.S. 60/426,256 under 35 U.S.C. §120 to ensure that the entry of the priority claim to the November 13, 2002 filing date of U.S. Provisional Patent Application U.S. 60/426,256.

REJECTIONS UNDER 35 USC §112, SECOND PARAGRAPH

Previously pending claims 10-13, 19-36, and 38 were rejected as indefinite for failure to provide a step comprising selection of a culture of cells that comprise replicating HCV RNA. Applicants have addressed this rejection with respect to Claims 10-13 by amending Claim 10 to

recite a step (b)“obtaining a culture of said cell line that supports replication of said genomic or subgenomic HCV RNA”. Support for this amendment can at least be found in Example 9 (which describes obtaining Huh-7.5 cell lines that support replication of subgenomic RNAs by selection), Example 10 (which describes obtaining Huh-7.5 cell lines that support replication of subgenomic HCV RNAs without selection; Page 15, line 24 -25), and Example 11 (which describes obtaining Huh-7.5 cell lines that support replication of genomic HCV RNAs without selection).

REJECTIONS UNDER 35 USC §112, FIRST PARAGRAPH

Previously pending claims 1-38 were rejected over alleged lack of enablement of claimed methods where the claims do not contain a requirement for selecting cells containing replicating HCV RNA or that are infected with HCV. Claims 1-9, 16, 17 and 37 were also rejected over alleged lack of enablement for methods where cells are infected with HCV. Claims 16, 17 and 37 were also rejected over alleged failure to satisfy the written description requirement.

As Claims 1-9, 16, 17 and 37 have been canceled by this amendment, the outstanding rejections of those claims for alleged lack of enablement are rendered moot. The cancellation of Claims 16, 17 and 37 also renders moot rejections of those claims over any alleged failure to satisfy the written description requirement.

As currently amended, Claim 10 specifies a step for obtaining a culture of an Huh-7.5 cell line that comprises a replicating genomic or subgenomic HCV RNA ((b)“obtaining a culture of said cell line that supports replication of said genomic or subgenomic HCV RNA”). As shown by the Examples, Applicants demonstrated that cultures of Huh-7.5 cell lines containing

replicating subgenomic HCV RNA could be obtained by transfecting Huh-7.5 cells with subgenomic HCV RNAs and either selecting for G418 resistant colonies (Page 14, lines 19-31) or by identifying transfected Huh-7.5 cells by FACS in the absence of selection (Page 15, line 20 to Page 16, line 21; Page 17, line 21-30). Applicants also demonstrated that Huh-7.5 cultures containing replicating genomic HCV RNA could be obtained by transfecting Huh-7.5 cells with genomic HCV RNA and identifying transfected Huh-7.5 cells by FACS in the absence of selection (Page 18, lines 6-31; Fig. 4). Applicants thus clearly enabled and demonstrated possession of a method where Huh-7.5 cell lines that support replication of subgenomic or genomic HCV RNAs could be obtained either in the presence or absence of selection and therefore respectfully request that the outstanding rejections over 35 U.S.C. §112, first paragraph be withdrawn.

REJECTIONS UNDER 35 USC §102

Examiner rejected then pending Claims 10-15, 18-36, and 38 under 35 U.S.C. §102(a) as anticipated by Blight et al. (J. Virol. 76:13001), alleging that this reference teaches both the methods claimed in the instant Application as well as the cell lines produced by those methods.

Applicant notes that the instant Application properly claims priority under 35 U.S.C. §119(e) and 35 U.S.C. § 120 to both the parent PCT Patent Application No. PCT/US2003/36634, filed November 13, 2003, and the U.S. Provisional Application No. 60/426,256, filed November 13, 2002, upon recognition of the priority claim by the Patent Office. A Petition under 37 C.F.R. §1.78(a)(3) was submitted on November 8, 2007 (copy enclosed) and all other requirements for establishing this priority claim have been met. As the November 13, 2002 filing

date of U.S. Provisional Application No. 60/426,256 precedes the December 2002 publication date of Blight et al., Blight et al. no longer qualifies as prior art with respect to this Application. Applicant therefore respectfully requests that the rejections of claims under 35 U.S.C. §102(a) over Blight et al. be withdrawn.

Examiner also rejected then pending Claims 10-15, 18-36, and 38 under 35 U.S.C. §102(e) as anticipated by DeFrancesco et al. (WO 02/059321), alleging that this reference teaches the both the methods claimed in the instant Application as well as the cell lines produced by those methods and the use of replicons comprising the S2204I adaptive mutation.

The claims as currently amended are directed to the Huh-7.5 cell line. DeFrancesco et al. does not anticipate the Huh-7.5 cell line. This Huh-7.5 cell line displays superior properties to other cell lines produced by the method of this Application, such as an ability to support extremely high transduction efficiencies (see Figure 2). While DeFrancesco et al report a method for obtaining "HCV replicon enhanced cells" that entails a curing step involving use of an antiviral agent, it is not clear that DeFrancesco et al. disclose all of the necessary cell culture conditions and parameters used by the Applicants to obtain the Huh-7.5 cell line. For example, the specification of the instant Application notes that "The most highly permissive sublines (Huh-7.5 and Huh-7.8) were obtained from G418-selected clones that harbored replicons without adaptive changes in the NS3-5B region (at the population sequence level)" (Page 4, Lines 7-9). Furthermore, it is clear from the description in the specification of the instant application that curing of any replicon containing cell line does not necessarily result in the production of a highly permissive cell line that supports increased levels or frequencies of HCV RNA replication. More specifically, the specification notes that "Curing of other replicon-containing

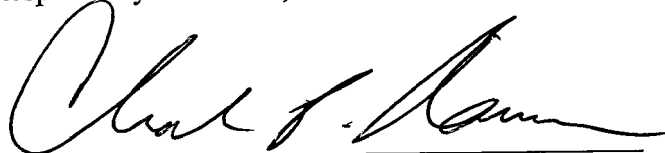
cell lines did not always yield a cell population that was more permissive for the replicons tested” (Page 4, line 12-13). The specification goes on to cite an example where a cured cell line failed to support improved levels of replication (Page 4, lines 13-16). Given these considerations, it is apparent that the general description of DeFrancesco et al. of a method involving a curing step and distinct cell lines isolated by the method of that application, does not anticipate the Huh-7.5 cell line and methods of using the Huh-7.5 cell line claimed herein. Applicant therefore respectfully requests that the rejections of the currently pending claims under 35 U.S.C. §102(e) over DeFrancesco et al. be withdrawn.

CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant, therefore, respectfully requests that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present Application is in condition for allowance. If the Examiner believes, for any reason, that a personal communication will expedite prosecution of this Application, he is invited to telephone the undersigned at the number provided.

It is not believed that extensions of time are required beyond those which may otherwise be provided for in documents accompanying this Response. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned for under 37 C.F.R. §1.136(a), and any fees required therefore are hereby authorized to be charged to our Deposit Account 20-0823.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Charles P. Romano", written over a horizontal line.

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Dated: November 8, 2007